	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	7783	igf-1 or (insulin-like adj growth adj factor)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:39			0
2	BRS	L2	2770	igf-1	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:39			0
3	BRS	L3	2022	insulin-like adj growth adj factor adj I	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:39			0
4	BRS	L4	2428	igf-I	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:40			0
5	BRS	L5	5346	2 or 3 or 4	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:46			0
6	BRS	L6	4997	low adj salt	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:46			0
7	BRS	L7	10	5 same 6	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:50			0
8	BRS	L8	3	7 same mg/ml same pH	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:52			0
9	BRS	L9	29493	sustained adj release	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:51			0
10	BRS	L10	101	5 same mg/ml same pH	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:52			0
11	BRS	L11	73713	arginine or guanidine	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:52			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
12	BRS	L12	9	10 same 11	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:53			0
13	BRS	L13	0	(7 or 12) same 9	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:54			0
14	BRS	L14	431	plga same microsphere	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:54			0
15	BRS	L15	0	(7 or 12) same 14	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:55			0
16	BRS	L16	32970	density same viscosity	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:55			0
17	BRS	L17	3	(7 or 12) same 16	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:55			0
18	BRS	L18	132719	kit	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:55			0
19	BRS	L19	3	(7 or 12) same 18	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:56			0
20	BRS	L20	14	shirley adj bret.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:56			0
21	BRS	L21	21	hora adj maninder.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:57			0
22	BRS	L22	0	(20 or 21) same 5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:57			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
23	BRS	L23	12	(20 or 21) and 5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/09/23 13:57			0

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=> file medline caplus biosis embase scisearch agricola
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'MEDLINE' ENTERED AT 14:11:56 ON 23 SEP 2003

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FILE 'SCISEARCH' ENTERED AT 14:11:56 ON 23 SEP 2003
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FILE 'AGRICOLA' ENTERED AT 14:11:56 ON 23 SEP 2003

=> s igf-1 or igf-i or (insulin-like growth factor 1)
L1        91061 IGF-1 OR IGF-I OR (INSULIN-LIKE GROWTH FACTOR 1)

=> s low salt
L2        16095 LOW SALT

=> s low (p) (arginine or guanidine)
L3        31154 LOW (P) (ARGININE OR GUANIDINE)

=> s l1 (p) (l2 or l3)
L4          329 L1 (P) (L2 OR L3)

=> s l4 (p) mg/ml (p) pH
'ML' IS NOT A VALID FIELD CODE
'ML' IS NOT A VALID FIELD CODE
'ML' IS NOT A VALID FIELD CODE
'ML' IS NOT A VALID FIELD CODE
L5            0 L4 (P) MG/ML (P) PH

=> s l4 (p) (mg per ml) (p) pH
L6            0 L4 (P) (MG PER ML) (P) PH

=> s l4 (p) concentration (p) pH
L7            1 L4 (P) CONCENTRATION (P) PH

=> d l7 1 ibib abs

L7   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         1999:325814  CAPLUS
DOCUMENT NUMBER:          130:343030
TITLE:                    Human IGF-I syrup composition and its use
INVENTOR(S):              Shirley, Bret A.; Hora, Maninder S.
PATENT ASSIGNEE(S):       Chiron Corporation, USA
SOURCE:                   PCT Int. Appl., 34 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   3
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 9924062         A1   19990520       WO 1998-US23672  19981106
         W:  AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
             CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, HR, HU,
             ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
             MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
             SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
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CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9913847 A1 19990[redacted] AU 1999-13847 19981[redacted]
EP 1028747 A1 20000823 EP 1998-957637 19981106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2001522813 T2 20011120 JP 2000-520150 19981106
US 2003109427 A1 20030612 US 1998-187661 19981106
PRIORITY APPLN. INFO.: US 1997-64891P P 19971107
US 1998-96081P P 19980811
WO 1998-US23672 W 19981106

AB A highly concd., ***low*** ***salt*** -contg., biol. active syrup form of ***IGF*** - ***I*** or variant thereof and methods for its prepn. are provided. This novel syrup form of ***IGF*** - ***I*** has an ***IGF*** - ***I*** ***concn*** . of at least about 250 mg/mL, a d. of about 1.0 g/mL to about 1.2 g/mL, and a viscosity of about 13,000 cP (cps) to about 19,000 cps, as measured at ambient temp. (23 .degree.C). The ***IGF*** - ***I*** syrup is prepd. by pptg. or partitioning ***IGF*** - ***I*** from soln., preferably by adjusting the soln. ***pH*** or by use of a soly. enhancer to conc. ***IGF*** - ***I*** in soln. followed by removal of the soly. enhancer. The pptd. syrup is useful as a means of storing ***IGF*** - ***I*** in a stable form and as a means of prepg. compns. comprising biol. active ***IGF*** - ***I*** . Pharmaceutical compns. and kits comprising this concd. ***IGF*** - ***I*** syrup are provided. The pptd. ***IGF*** - ***I*** syrup, ***IGF*** - ***I*** reconstituted from the ***IGF*** - ***I*** syrup, pharmaceutical compns., and kits are useful in ***IGF*** - ***I*** therapy directed to ***IGF*** - ***I*** -responsive conditions.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 14:11:33 ON 23 SEP 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 14:11:56 ON 23 SEP 2003
L1 91061 S IGF-1 OR IGF-I OR (INSULIN-LIKE GROWTH FACTOR 1)
L2 16095 S LOW SALT
L3 31154 S LOW (P) (ARGININE OR GUANIDINE)
L4 329 S L1 (P) (L2 OR L3)
L5 0 S L4 (P) MG/ML (P) PH
L6 0 S L4 (P) (MG PER ML) (P) PH
L7 1 S L4 (P) CONCENTRATION (P) PH

=> s sustained release
L8 45331 SUSTAINED RELEASE

=> s plga (p) microsphere
L9 2146 PLGA (P) MICROSPHERE

=> s density same viscosity
L10 0 DENSITY SAME VISCOSITY

=> s density (p) viscosity
L11 15677 DENSITY (P) VISCOSITY

=> s kit
L12 110187 KIT

=> s l4 (p) l8
L13 0 L4 (P) L8

=> s l4 (p) l9
L14 0 L4 (P) L9

=> s l4 (p) l11
L15 0 L4 (P) L11

=> s l4 (p) l12
L16 1 L4 (P) L12

=> s l16 not l7
L17 0 L16 NOT L7

=> s shirley bret/au

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L18          6 SHIRLEY BRET/AU

=> s hora maninder/au
L19         16 HORA MANINDER/AU

=> s (l18 or l19) and l4
L20          0 (L18 OR L19) AND L4

=> s l19 and l1
L21          7 L19 AND L1

=> d l21 1-7 ibib abs

L21  ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         1999:325813  CAPLUS
DOCUMENT NUMBER:          130:343029
TITLE:                    Method for producing   ***IGF***  -  ***1***
                          sustained-release formulations
INVENTOR(S):              Shirley, Bret;   ***Hora, Maninder***  ; O'Hagan,
                          Derek; Singh, Manmohan
PATENT ASSIGNEE(S):       Chiron Corporation, USA
SOURCE:                   PCT Int. Appl., 60 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   3
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     --------------    ----  --------       ---------------   --------
     WO 9924061         A1   19990520       WO 1998-US23627   19981106
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE,
             KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,
             MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
             TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9913841         A1   19990531       AU 1999-13841     19981106
     EP 1028746         A1   20000823       EP 1998-957624    19981106
     EP 1028746         B1   20030226
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     JP 2001522812      T2   20011120       JP 2000-520149    19981106
     US 2002013273      A1   20020131       US 1998-187780    19981106
     US 6573238         B2   20030603
     AT 233097          E    20030315       AT 1998-957624    19981106
PRIORITY APPLN. INFO.:                    US 1997-64891P    P  19971107
                                          US 1998-96066P    P  19980811
                                          WO 1998-US23627   W  19981106
AB   Methods for prepg. biodegradable poly(D,L-lactide-co-glycolide)
     microparticles are provided.  Also provided are microparticles prepd. by
     the method which include   ***IGF***  -  ***1***   entrapped therein.  The
     microparticles allow for controlled release of   ***IGF***  -  ***1***
     and other polypeptides over prolonged periods of time.
REFERENCE COUNT:          3     THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21  ANSWER 2 OF 7  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         1999:193979  CAPLUS
DOCUMENT NUMBER:          130:227745
TITLE:                    High and low load formulations of   ***IGF***  -
                            ***I***   in multivesicular liposomes
INVENTOR(S):              Shirley, Bret A.;   ***Hora, Maninder***  ; Ye, Qiang;
                          Katre, Nandini; Asherman, John
PATENT ASSIGNEE(S):       Depotech Corporation, USA; Chiron Corporation
SOURCE:                   PCT Int. Appl., 59 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     --------------    ----  --------       ---------------   --------
     WO 9912522         A1   19990318       WO 1998-US18738   19980908
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W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6306432	B1	20011023	US 1997-925531	19970908
AU 9893100	A1	19990329	AU 1998-93100	19980908
EP 1021167	A1	20000726	EP 1998-945974	19980908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001515852	T2	20010925	JP 2000-510421	19980908

PRIORITY APPLN. INFO.: US 1997-925531 A1 19970908
WO 1998-US18738 W 19980908

AB Disclosed are multivesicular liposomes (MVLs) contg. ***IGF*** - ***I*** with substantially full bioavailability, wherein the loading of the ***IGF*** - ***I*** into the liposomes is modulated by adjusting the osmolarity of the aq. component into which the agents are dissolved prior to encapsulation. In the making of MVLs, the process involves dissolving the ***IGF*** - ***I*** , an osmolarity excipient, and a pH modifying agent sufficient to solubilize the ***IGF*** - ***I*** in a first aq. component used during manuf. of the MVLs. To increase the loading of the ***IGF*** - ***I*** , the osmolarity of the aq. component used during manuf. of the MVLs is reduced, whereas the osmolarity of the aq. component is increased to obtain the low load formulations. The rate of release of the active agent into the surrounding environment in which the liposomes are introduced can be simultaneously controlled by incorporating into the lipid component used in the formulation at least one long chain amphipathic lipid. Use of the long chain amphipathic lipid in the lipid component is particularly helpful in controlling the release rate from high drug load formulations. A water-in-oil prepn. was prepd. by mixing a lipid component comprising 1,2-dioleoyl-sn-glycero-3-phosphocholine 13.20, cholesterol 19.88, 1,2-dipalmitoyl-sn-glycero-3-phosphocholine 2.79, and triolein 2.44 mM in chloroform with an aq. component comprising IFG-I 20 mg/mL, sucrose 5.0%, and HCl 100 mM. The drug loading of the final liposome suspension was 37.7%.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:491200 CAPLUS
DOCUMENT NUMBER: 129:265361
TITLE: Multivesicular Liposome (DepoFoam) Technology for the Sustained Delivery of Insulin-like Growth Factor-I (***IGF*** - ***I***)
AUTHOR(S): Katre, Nandini V.; Asherman, John; Schaefer, Heather; ***Hora, Maninder***
CORPORATE SOURCE: DepoTech Corporation, San Diego, CA, 92121, USA
SOURCE: Journal of Pharmaceutical Sciences (1998), 87(11), 1341-1346
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Insulin-like Growth Factor I (***IGF*** - ***I***), a 7.65 kD protein which has a variety of metabolic functions, is being evaluated for its therapeutic benefit in several disease states. To sustain therapeutic blood levels in a no. of these instances, ***IGF*** - ***I*** needs to be administered repeatedly. The development of a sustained-release depot delivery system for this protein which would replace repeated administration was studied. Using a multivesicular liposome drug delivery system (DepoFoam), sustained delivery kinetics have been obsd. for ***IGF*** - ***I*** . ***IGF*** - ***I*** was successfully encapsulated in this system with good efficiency. The integrity of the encapsulated protein was maintained, as characterized by physiochem. (HPLC, SDS-PAGE), and by biol. methods (mitogenic activity). The DepoIGF-I particles were also characterized by their morphol. (particles were smooth, multivesicular, and there was no debris), particle size (ranged from 18 to 20 .mu.m), and in vitro and in vivo release kinetics of ***IGF*** - ***I*** . The DepoIGF-I particles released the protein drug in a sustained manner both in vitro and in vivo without a rapid initial release, and the released protein maintained its structural integrity and biol. activity. The in vitro studies in human plasma at 37.degree.C showed that the DepoIGF-I particles released ***IGF*** -

I slowly over several days; 70-80% of the protein was released in 6-7 days. In a pharmacokinetic in vivo study, after s.c. injections in rats, ***IGF*** - ***I*** levels were sustained for 5-7 days with DepoIGF-I formulation, whereas ***IGF*** - ***I*** in the free form was cleared in 1 day. DepoFoam technol. provides a pharmaceutically useful system of sustained delivery for proteins, which can be extended to other therapeutic macromols.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 4 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:313118 BIOSIS
DOCUMENT NUMBER: PREV200300313118
TITLE: Method for producing sustained-release formulations.
AUTHOR(S): Shirley, Bret; ***Hora, Maninder*** ; O'Hagan, Derek; Singh, Manmohan
ASSIGNEE: Chiron Corporation
PATENT INFORMATION: US 6573238 June 03, 2003
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (June 3 2003) Vol. 1271, No. 1, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB Methods for preparing biodegradable microparticles are provided. Also provided are microparticles prepared by the method which include ***IGF*** - ***1*** entrapped therein. The microparticles allow for controlled release of ***IGF*** - ***1*** and other polypeptides over prolonged periods of time.

L21 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:6292 BIOSIS
DOCUMENT NUMBER: PREV200200006292
TITLE: High and low load formulations of ***IGF*** - ***I*** in multivesicular liposomes.
AUTHOR(S): Shirley, Bret (1); ***Hora, Maninder*** ; Ye, Qiang; Katre, Nandini; Asherman, John
CORPORATE SOURCE: (1) Concord, CA USA
ASSIGNEE: Chiron Corporation; SkyePharma Inc.
PATENT INFORMATION: US 6306432 October 23, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 23, 2001) Vol. 1251, No. 4, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB Disclosed are multivesicular liposomes (MVLs) containing ***IGF*** - ***I*** with substantially full bioavailability, wherein the loading of the ***IGF*** - ***I*** into the liposomes is modulated by adjusting the osmolarity of the aqueous component into which the agents are dissolved prior to encapsulation. In the making of MVLs, the process involves dissolving the ***IGF*** - ***I*** , an osmolarity excipient, and a pH modifying agent sufficient to solubilize the ***IGF*** - ***I*** in a first aqueous component used during manufacture of the MVLs. To increase the loading of the ***IGF*** - ***I*** , the osmolarity of the aqueous component used during manufacture of the MVLs is reduced, whereas the osmolarity of the aqueous component is increased to obtain the low load formulations. The rate of release of the active agent into the surrounding environment in which the liposomes are introduced can be simultaneously controlled by incorporating into the lipid component used in the formulation at least one long chain amphipathic lipid. Use of the long chain amphipathic lipid in the lipid component is particularly helpful in controlling the release rate from high drug load formulations.

L21 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:25641 BIOSIS
DOCUMENT NUMBER: PREV199900025641
TITLE: Multivesicular liposome (DepoFoam) technology for the sustained delivery of insulin-like growth factor-I (***IGF*** - ***I*** .
AUTHOR(S): Katre, Nandini V. (1); Asherman, John; Schaefer, Heather; ***Hora, Maninder***
CORPORATE SOURCE: (1) DepoTech Corp., 10450 Science Center Drive, San Diego, CA 92121 USA
SOURCE: Journal of Pharmaceutical Sciences, (Nov., 1998) Vol. 87,

No. 11, pp. 1341-1346.
ISSN: 0022-35[redacted]
DOCUMENT TYPE: Article
LANGUAGE: English
AB Insulin-like Growth Factor I (***IGF*** - ***I***), a 7.65 kD protein which has a variety of metabolic functions, is being evaluated for its therapeutic benefit in several disease states. To sustain therapeutic blood levels in a number of these instances, ***IGF*** - ***I*** needs to be administered repeatedly. The objective of these studies was the development of a sustained-release depot delivery system for this protein which would replace repeated administration. Using a multivesicular liposome drug delivery system (DepoFoam), sustained delivery kinetics have been observed for ***IGF*** - ***I*** . ***IGF*** - ***I*** was successfully encapsulated in this system with good efficiency. The integrity of the encapsulated protein was maintained, as characterized by physicochemical (HPLC, SDS-PAGE), and by biological methods (mitogenic activity). The DepoIGF-I particles were also characterized by their morphology (particles were smooth, multivesicular, and there was no debris), particle size (ranged from 18 to 20 mum), and in vitro and in vivo release kinetics of ***IGF*** - ***I*** . The DepoIGF-I particles released the protein drug in a sustained manner both in vitro and in vivo without a rapid initial release, and the released protein maintained its structural integrity and biological activity. The in vitro studies in human plasma at 37 degreeC showed that the DepoIGF-I particles released ***IGF*** - ***I*** slowly over several days; 70-80% of the protein was released in 6-7 days. In a pharmacokinetic in vivo study, after subcutaneous injections in rats, ***IGF*** - ***I*** levels were sustained for 5-7 days with DepoIGF-I formulation, whereas ***IGF*** - ***I*** in the free form was cleared in 1 day. DepoFoam technology provides a pharmaceutically useful system of sustained delivery for proteins, which can be extended to other therapeutic macromolecules.

L21 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1997:6747 BIOSIS
DOCUMENT NUMBER: PREV199799305950
TITLE: A lipid-based multivesicular controlled-release system for the delivery of insulin-like growth factor (***IGF*** - ***1*** .
AUTHOR(S): Katre, Nandini V. (1); Asherman, John (1); Schaefer, Heather (1); ***Hora, Maninder***
CORPORATE SOURCE: (1) DepoTech Corp., 10450 Science Center Drive, San Diego, CA 92121 USA
SOURCE: Pharmaceutical Research (New York), (1996) Vol. 13, No. 9 SUPPL., pp. S77.
Meeting Info.: Annual Meeting of the American Association of Pharmaceutical Scientists Seattle, Washington, USA October 27-31, 1996
ISSN: 0724-8741.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English

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(FILE 'HOME' ENTERED AT 14:11:33 ON 23 SEP 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 14:11:56 ON 23 SEP 2003

L1	91061	S IGF-1 OR IGF-I OR (INSULIN-LIKE GROWTH FACTOR 1)
L2	16095	S LOW SALT
L3	31154	S LOW (P) (ARGININE OR GUANIDINE)
L4	329	S L1 (P) (L2 OR L3)
L5	0	S L4 (P) MG/ML (P) PH
L6	0	S L4 (P) (MG PER ML) (P) PH
L7	1	S L4 (P) CONCENTRATION (P) PH
L8	45331	S SUSTAINED RELEASE
L9	2146	S PLGA (P) MICROSPHERE
L10	0	S DENSITY SAME VISCOSITY
L11	15677	S DENSITY (P) VISCOSITY
L12	110187	S KIT
L13	0	S L4 (P) L8
L14	0	S L4 (P) L9
L15	0	S L4 (P) L11
L16	1	S L4 (P) L12
L17	0	S L16 NOT L7
L18	6	S SHIRLEY BRET/AU
L19	16	S HORA MANINDER/AU

L20 0 S (L18 OR L19) AND L4
L21 7 S L19 AND L1

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	85.11	85.32

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.60	-2.60

STN INTERNATIONAL LOGOFF AT 14:20:49 ON 23 SEP 2003